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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/019,100
Filing Date: August 21, 2003
Appellant(s): SAIDI ET AL.

Vyacheslav V. Vasilyev
For Appellant

EXAMINER'S ANSWER

This is in response to the supplemental appeal brief filed March 2, 2010 appealing from the Office action mailed April 15, 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

WITHDRAWN REJECTIONS

In view of the Approved Terminal Disclaimer, the following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

The rejection of claims 1, 6, 10, 12-17, and 22-27 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6241969 B1.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,193,985	Sonne	2-2001

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 10, 13-17 and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sonne (US Pat No. 6,193,985– previously presented).

The invention reads on a composition consisting of: (a) from 5 ug/mL to about 5 mg/mL of a corticosteroid in dissolved form; (b) from about 0.1 to 20 percent by weight of a pharmaceutically acceptable, high-HLB surfactant component, wherein the HLB of the surfactants present in the high HLB surfactant component comprises at least 50%

by weight of an ethoxylated derivative of vitamin E, wherein said ethoxylated derivative of vitamin E is the sole vitamin E component of the composition; and (c) at least about 70 weight percent aqueous phase.

Sonne discloses an oil in water emulsion of budesonide as nose drop or nasal spray, comprising in the oily phase 0.025 grams of budesonide, 5 grams of vitamin e TPGS and 12.5 grams alpha-tocopherol – (viscous oil (surfactant)) (see col 3 line 18, col 11 Example 15). The limitation of the composition having at least about 70 weight percent of aqueous phase is met by the teachings of the water phase in the prior art (col 11 Example 15). Additionally, Sonne et al. teaches "Generally speaking compositions of the invention may contain from 1 to 99.99% (w/w), preferably 20 to 99.99%, most preferably 40 to 99.99% (w/w) of the tocopherol or tocopherol derivative solvent. The emulsion used in compositions of the invention may contain 1 to 95% (w/w) of the tocopherol or derivative thereof, preferably 20 to 95% (w/w), most preferably 35 to 80% (w/w) (Col 5 lines 55-61)." Sonne teaches "the formulations according to the invention may be optimized with respect to bioadhesion, sprayability and viscosity, as desired. Thus for example, the following co-solvents may be added: Vegetable oils such as sesame- or olive- or fractionated coconut oil, alcohols such as ethanol, propylene glycol, glycerol, polyethylene glycol or benzyl alcohol; or triacetin, (col 6 lines 47-59)" meeting the limitation of claims 15 and 17. Further, Sonne teaches "the tocopherol derivative emulsifier of the invention may be used alone or in conjunction with other known emulsifiers eg. phospholipids, polysorbates, sorbitan esters of fatty acids, cetearyl glucoside or poloxamers. It has furthermore surprisingly been shown that various other

solvents may be used in the emulsion system described above, without compromising the stability of the emulsion (col 4 lines 50-56)."

Sonne fails to exemplify a composition "wherein said ethoxylated derivative of vitamin E is the sole vitamin E component of the composition," or comprising a high-HLB surfactant component of at least 50%, 75%, 90% by weight tocopheryl polyethylene glycol 1000 succinate. Further, Sonne does not exemplify a composition containing from about 0.1 to about 20 percent by weight of a pharmaceutically acceptable cosolvent comprising propylene glycol, polyethylene glycol having a molecular weight between about 200 and 4000, glycerol, ethoxydiglycol, glycofurol, and ethanol, or a combination thereof, 0.1 to about 3 percent by weight of phospholipids, nor 0.1 to about 3 percent by weight of an oil.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the composition by substituting the alpha-tocopherol of Example 15 with a vitamin e-TPGS and incorporating additional ingredients such as oils or alcohols inclusive of ethanol, propylene glycol, glycerol, polyethylene glycol or benzyl alcohol; or triacetin, or emulsifiers eg. phospholipids, polysorbates, sorbitan esters of fatty acids, cetearyl glucoside or poloxamers. The motivation to make such an incorporation is because Sonne teaches (1) it has been surprisingly found "that tocopherol derivatives, particularly certain esters, may themselves form efficient, non-irritating emulsifiers to enable stable emulsions to be formed, even where high lipid levels are involved eg. about 50-70%. Particular mention may be made in this regard of Vitamin E TPGS which is a water soluble derivative of Vitamin E and consists of .alpha.-

tocopherol, which is esterified with succinic acid, the other acidic group of the latter being esterified with polyethylene glycol 1000. Vitamin E TPGS is an almost odourless waxy amphiphilic substance with a molecular weight about 1513 (col 4, lines 27-35);" (2) the formulations according to the invention may be optimized with respect to bioadhesion, sprayability and viscosity, as desired. Thus for example, the following co-solvents may be added: Vegetable oils such as sesame- or olive- or fractionated coconut oil, alcohols such as ethanol, propylene glycol, glycerol, polyethylene glycol or benzyl alcohol; or triacetin and (3) the tocopherol derivative emulsifier of the invention may be used alone or in conjunction with other known emulsifiers eg. phospholipids, polysorbates, sorbitan esters of fatty acids, cetearyl glucoside or poloxamers. It has furthermore surprisingly been shown that various other solvents may be used in the emulsion system described above, without compromising the stability of the emulsion. Hence, the skilled artisan would have had reasonable expectation of successfully producing a composition that is non-irritating with optimized bioadhesion, sprayability, viscosity, without compromising the stability of the emulsion.

Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the dose range of the Sonne composition by routine experimentation (see 2144.05 11). The motivation to optimize the dose range of the Sonne 's final formulation is because one would have had a reasonable expectation of success in achieving the safest clinical outcome.

The composition "suitable for administering a therapeutic dose of a corticosteroid to the respiratory tract" is an intended use and does not receive patentable weight in a composition claim.

(10) Response to Argument

A prima facie case of obviousness has been established. Appellant argues that a prima facie case of obviousness has not been established. Particularly, Appellant argues that (a) the 'consisting of' language excludes components that are recited in the Sonne reference.. In response, the Examiner states Sonne teaches vitamin E TPGS is a tocopherol derivative (see col. 4 lines 33-35). Additionally, the reference teaches an embodiment of the invention wherein the biologically active agent is dissolved in tocopherol or a derivative thereof (col 6 lines 18-23). Hence, taking the disclosure of the reference as a whole, the composition of Sonne can have either an alpha tocopherol (vitamin E) or a derivative thereof, such as Vitamin E TPGS.

Appellant further argues that (b) Sonne has made a distinction between tocopherol derivative solvents and emulsifiers and that the reference does not teach the removal of the tocopherol-based solvent, alpha tocopherol (vitamin E). The Examiner respectfully reiterates that Sonne clearly discloses "the use of a tocopherol or a derivative thereof as a solvent **and/or** emulsifier for substantially insoluble and sparingly soluble biologically active agents, especially in the manufacture of pharmaceutical compositions (see abstract)." Although the reference does not exemplify the sole use of vitamin E TPGS in a composition, one of ordinary skill in the art would have been motivated to utilize a

tocopherol derivative in order to produce an efficient, non-irritating, and stable emulsion because Sonne teaches the use of a tocopherol or a derivative thereof.

The Appellant argues (c) "there is no reasonable expectation of success from Sonne that the use of the vitamin E-TPGS emulsifier as a sole vitamin E compound is sufficient to administer insoluble drugs in a stable emulsion." The Examiner's position is that Sonne's exemplified emulsion comprising budesonide (corticosteroid), alpha tocopherol (vitamin E), vitamin E TPGS (high HLB surfactant component comprising at least 50% by wt of an ethoxylated derivative of vitamin E of claim 1, part (b)), and a water phase (claim 1, part (c)), in combination with the teaching that "the use of a tocopherol or a derivative thereof as a solvent **and/or** emulsifier for substantially insoluble and sparingly soluble biologically active agents, especially in the manufacture of pharmaceutical compositions (see abstract)," renders obvious the claimed invention.

Appellant argues(d) "replacement of tocopherol with vitamin E TPGS in the composition of Sonne is not routine experimentation because Sonne never disclosed the basic conditions of the instant claims." "Sonne does not suggest removal of an alpha-tocopherol based solvent from his composition." The Examiner respectfully repeats "the use of a tocopherol or a derivative thereof as a solvent **and/or** emulsifier for substantially insoluble and sparingly soluble biologically active agents, especially in the manufacture of pharmaceutical compositions (see abstract)." The Appellant argues the solvent must be present in a functionally meaningful amount to dissolve the active agent. If the solvent is absent then the active agent is not dissolved because the vitamin E TPGS is a water soluble substance. The Examiner points to the teaching in

Sonne wherein vitamin E TPGS is only about 20% soluble in water (see col 4 line 40). Therefore, it remains the Examiners contention that it would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the composition by substituting the alpha-tocopherol of Example 15 with a vitamin e-TPGS, as described in the rejection above.

With respect to claim 15, the Appellant argues (a) the tocopherol-based solvents are excluded from the claim. Additionally, the Appellant argues the Sonne reference teaches the tocopherol-based solvents in the examples. The Examiner respectfully reiterates that Sonne clearly discloses “the use of a tocopherol or a derivative thereof as a solvent **and/or** emulsifier for substantially insoluble and sparingly soluble biologically active agents, especially in the manufacture of pharmaceutical compositions (see abstract).” The argument that Sonne discloses co-solvents that are used in addition to the tocopherol-based solvent, and a composition lacking the tocopherol-based solvent falls outside of Sonne’s framework is not persuasive. Claim 15 is drawn to a composition comprising a "co-solvent." The Examiner states the reference clearly teaches that the tocopherol derivative emulsifiers may be used alone or in conjunction with other known emulsifiers; and, it has furthermore surprisingly been shown that various other solvents may be used in the emulsion system described above, without compromising the stability of the emulsion, (see col 4 lines 50-56). Hence, the skilled artisan would have had a reasonable expectation of successfully producing a composition that is non-irritating with optimized bioadhesion, sprayability, and viscosity, without compromising the stability of the emulsion (see col 4 lines 50-56).

With respect to claim 17, Appellant argues (a) the tocopherol-based solvents are excluded from the claims. Additionally, the Appellant argues the Sonne reference teaches the tocopherol-based solvents in the examples. The Examiner respectfully reiterates that Sonne clearly discloses "the use of a tocopherol or a derivative thereof as a solvent **and/or** emulsifier for substantially insoluble and sparingly soluble biologically active agents, especially in the manufacture of pharmaceutical compositions (see abstract)."

Additionally, Appellant's argument that Sonne teaches "triglycerides such as vegetable oils are generally non-irritant, but usually these oils are too poor as solvents to be of any use" is not persuasive. The Examiner states that Appellant has pointed to the background teachings of Sonne. The Sonne reference teaches vegetable oils are useful for the purpose of optimizing bioadhesion, sprayability and viscosity, as desired (col 6 lines 45-55). In this case, a skilled artisan would not deter from using triglycerides as a solvent.

The objective evidences on the record are not sufficient to overcome the obviousness rejections.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

Conferees:

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616

/Layla Soroush/
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